U.S. Serial No.: 09/896,856 Amdt. Dated November 24, 2003

Response to Final Office Action mailed on May 23, 2003

## Amendments to the Specification:

Please amend the specification to read as follows wherein strikeout in brackets [00] indicates deleted terminology and underling, 00, indicates added terminology.

Please replace the paragraph beginning at page 5, line 26, with the following rewritten paragraph:

In another aspect, the isolated CHF polypeptide shares at least 75% amino acid sequence identity with the translated CHF sequence shown in Fig. 1 (SEQ ID NO:3). In a further aspect, the polypeptide is the mature human CHF having the translated CHF sequence shown in Fig. 5 (SEQ ID NO:8).

Please replace the paragraph beginning at page 5, line 31, with the following rewritten paragraph:

In a still further aspect, the invention provides an isolated polypeptide encoded by a nucleic acid having a sequence that hybridizes under moderately stringent conditions to the nucleic acid sequence provided in Fig. 1 (SEQ ID NO:1 or 2). Preferably, this polypeptide is biologically active.

Please replace the paragraph beginning at page 6, line 28, with the following rewritten paragraph:

In additional aspects, the invention provides an isolated nucleic acid molecule comprising the open reading frame nucleic acid sequence shown in Fig. 1 (SEQ ID NO:1 or 2) or Fig. 5 (SEQ ID NO:6 or 7). The invention also provides an isolated nucleic acid molecule excluding rat CHF selected from the group consisting of:

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Please replace the paragraph beginning at page 9, line 24, with the following rewritten paragraph:

"CHF variants" or "CHF sequence variants" as defined herein mean biologically active CHFs as defined below having less than 100% sequence identity with the CHF isolated from recombinant cell culture or from murine embryoid bodies having the deduced sequence described in Fig. 1 (SEQ ID NO:3), or with the human equivalent described in Fig. 5 (SEQ ID NO:8). Ordinarily, a biologically active CHF variant will have an amino acid sequence having at least about 70% amino acid sequence identity with the CHF isolated from murine embryoid bodies or the mature human CHF (see Figs. 1 (SEQ ID NO:3) and 5 (SEQ ID NO:8)), preferably at least about 75%, more preferably at least about 80%, still more preferably at least about 85%, even more preferably at least about 90%, and most preferably at least about 95%.

Please replace the paragraph beginning at page 11, line 1, with the following rewritten paragraph:

An "antigenic function" means possession of an epitope or antigenic site that is capable of cross-reacting with antibodies raised against the native CHF whose sequence is shown in Fig. 1 (SEQ ID NO:3) or another mammalian native CHF, including the human homolog whose sequence is shown in Fig. 5 (SEQ ID NO:8). The principal antigenic function of a CHF polypeptide is that it binds with an affinity of at least about 10<sup>6</sup> L/mole to an antibody raised against CHF isolated from mouse embryoid bodies or a human homolog thereof. Ordinarily, the polypeptide binds with an affinity of at least about 10<sup>7</sup> L/mole. Most preferably, the antigenically active CHF polypeptide is a polypeptide that binds to an antibody raised against CHF having one of the above-described effector functions. The antibodies used to define "biologically activity" are rabbit polyclonal antibodies raised by formulating the CHF isolated from recombinant cell culture or embryoid bodies in Freund's complete adjuvant, subcutaneously injecting the formulation, and boosting the immune response by intraperitoneal injection of the formulation until the titer of the anti-CHF antibody plateaus.

U.S. Serial No.: 09/896,856 Amdt. Dated November 24, 2003

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Please replace the paragraph beginning at page 12, line 25, with the following rewritten paragraph:

"Percent amino acid sequence identity" with respect to the CHF sequence is defined herein as the percentage of amino acid residues in the candidate sequence that are identical with the residues in the CHF sequence isolated from murine embryoid bodies having the deduced amino acid sequence described in Fig. 1 (SEQ ID NO:3) or the deduced human CHF amino acid sequence described in Fig. 5 (SEQ ID NO:8), after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. None of N-terminal, C-terminal, or internal extensions, deletions, or insertions into the CHF sequence shall be construed as affecting sequence identity or homology. Thus, exemplary biologically active CHF polypeptides considered to have identical sequences include prepro-CHF, pro-CHF, and mature CHF.

Please replace the paragraph beginning at page 26, line 16, with the following rewritten paragraph:

Optional preferred polypeptides of this invention are biologically active CHF variant(s) with an amino acid sequence having at least 70% amino acid sequence identity with the murine CHF of Fig. 1 (SEQ ID NO:3), preferably at least 75%, more preferably at least 80%, still more preferably at least 85%, even more preferably at least 90%, and most preferably at least 95% (*i.e.*, 70-100%, 75-100%, 80-100%, 85-100%, 90-100%, and 95-100% sequence identity, respectively). Alternatively, the preferred biologically active CHF variant(s) have an amino acid sequence having at least 70%, preferably at least 75%, more preferably at least 80%, still more preferably at least 85%, even more preferably at least 90%, and most preferably at least 95% amino acid sequence identity with the human CHF sequence of Fig. 5 (SEQ ID NO:8) (i.e., 70-100%, 75-100%, 80-100%, 85-100%, 90-100%, and 95-100% sequence identity, respectively).

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Please replace the paragraph beginning at page 27, line 1, with the following rewritten paragraph:

More preferred CHF polypeptides are those encoded by genomic DNA or cDNA and having the amino acid sequence of murine CHF described in Fig. 1 (SEQ ID NO:3) or the amino acid sequence of human CHF described in Fig. 5 (SEQ ID NO:8).

Please replace the paragraph beginning at page 29, line 33, with the following rewritten paragraph:

More preferred isolated nucleic acid molecules are DNA sequences encoding biologically active CHF, selected from: (a) DNA based on the coding region of a mammalian CHF gene (e.g., DNA comprising the nucleotide sequence provided in Fig. 1 (SEQ ID NO:1 or 2) or Fig. 5 (SEQ ID NO:6 or 7), or fragments thereof); (b) DNA capable of hybridizing to a DNA of (a) under at least moderately stringent conditions; and (c) DNA that is degenerate to a DNA defined in (a) or (b) which results from degeneracy of the genetic code. It is contemplated that the novel CHFs described herein may be members of a family of ligands having suitable sequence identity that their DNA may hybridize with the DNA of Fig. 1 (SEQ ID NO:1 or 2) or Fig. 5 (SEQ ID NO:6 or 7) (or fragments thereof) under low to moderate stringency conditions. Thus, a further aspect of this invention includes DNA that hybridizes under low to moderate stringency conditions with DNA encoding the CHF polypeptides.

Please replace the paragraph beginning at page 33, line 27, with the following rewritten paragraph:

Amino acid sequence variants of native CHF are prepared by introducing appropriate nucleotide changes into the native CHF DNA, or by *in vitro* synthesis of the desired CHF polypeptide. Such variants include, for example, deletions from, or insertions or substitutions of, residues within the amino acid sequence shown for murine CHF in Figure 1 (SEQ ID NO:3) and for human CHF in Figure 5 (SEQ ID NO:8). Any combination of deletion, insertion, and substitution is made to arrive at the final construct, provided that the final construct possesses the desired characteristics. Excluded from the scope of this invention are CHF variants or polypeptide sequences that

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are the rat homolog of CHF. The amino acid changes also may alter post-translational processes of the native CHF, such as changing the number or position of glycosylation sites.

Please replace the paragraph beginning at page 66, line 34, with the following rewritten paragraph:

Alternatively, using the murine sequence shown in Figure 1 (SEQ ID NO:3) or the human sequence shown in Figure 5 (SEQ ID NO:8), variants of native CHF are made that act as antagonists. Since the GH/cytokine receptor family is known to have two binding sites on the ligand, the receptor binding sites of CHF can be determined by binding studies and one of them eliminated by standard techniques (deletion or radical substitution) so that the molecule acts as an antagonist.